June 2, 2003

Connie L. Deford
Global Environment, Health & Safety Manager
The Dow Chemical Company
1691 North Swede
Midland, MI 48674

Dear Ms. Deford:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Alkyl Diphenyl Oxide Disulfonates (ADPODS) posted on the ChemRTK HPV Challenge Program Web site on January 22, 2003. I commend The Dow Chemical Company for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The Dow Chemical Company advise the Agency, within 90 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Alkyl Diphenyl Oxide Disulfonates (ADPODS) Category

Summary of EPA Comments

The sponsor, the Dow Chemical Company, submitted a test plan and robust summaries to EPA for Alkyl Diphenyl Oxide Disulfonates (ADPODS) category dated December 20, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 22, 2003. The category consists of five sponsored HPV substances. Information on two non-HPV substances is also provided as supporting data.

EPA has reviewed this submission and has reached the following conclusions:

1. Category Justification. The data provided by the submitter generally support the category.

2. Physicochemical Properties. The data provided by the submitter for melting point, boiling point, vapor pressure and octanol/water partition coefficient are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide water solubility data.

3. Environmental Fate. The submitter needs to incorporate the photodegradation and stability in water information in the robust summaries. The submitter needs to provide ready biodegradation data for the C12 linear salt. EPA recommends that the submitter provide transport and distribution (fugacity) data using a level III model.

4. Health Effects. Adequate data are available for acute, repeated-dose and genetic toxicities for the purposes of the HPV Challenge Program. EPA agrees with the submitter's plan and recommends a combined reproduction/developmental screening test on C6 and C16 linear sodium salts to define the category boundaries. The submitter needs to address deficiencies in the robust summaries.

5. Ecological Effects. The data for fish and invertebrates are adequate for the purposes of the HPV Challenge Program. The data for algal studies are inadequate and further testing is necessary. EPA reserves judgement on the adequacy of the chronic daphnia reproduction studies pending submission of additional information.

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.

EPA Comments on the Alkyl Diphenyl Oxide Disulfonates (Adpods)
Challenge Submission

Category Definition

The submitter proposed a category of five substances containing predominantly monoalkylated derivatives of diphenyl oxide disulfonates. Each phenyl group of the diphenyl oxide contains a linear or branched alkyl group with carbon numbers of C6, C10, or C12. The alkyl groups are linear aliphatic hydrocarbons, which are bonded to the phenyl groups through the second carbon in the aliphatic hydrocarbon chain. These substances also contain the following minor components: dialkylated derivatives of diphenyl oxide disulfonate, and mono- and dialkylated derivatives of diphenyl oxide monosulfonates.

There are five HPV substances in the category:

1) Decyl(sulfophenoxy)benzenesulfonic acid (CAS No. 70191-75-2): C10 linear acid;
2) Decyl(sulfophenoxy)benzenesulfonic acid, disodium salts (CAS No. 36445-71-3): C10 linear, Na salt;
3) *sec*-Dodecyl derivatives of sulfonated 1,1'-oxybisbenzene (CAS No. 149119-20-0): C12 linear, Na salt;
4) Tetrapropylene derivatives of sulfonated 1,1'-oxybisbenzene (CAS No.119345-03-8): C12 branched

acid;
5) Tetrapropylene derivatives of sulfonated 1,1'-oxybisbenzene, sodium salts (CAS No. 119345-04-9): C12 branched, Na salt.

The submitter also provides test data on two non-HPV substances in support of the category: C6 linear, Na salt (CAS No. 147732-60-3) and C16 linear, Na salt (CAS No. 65143-89-7). There is an eighth substance included in the main list of category members on p. 7 of the test plan, dodecyl(sulfophenoxy)-benzenesulfonic acid, disodium salts (CAS No. 28519-02-0), which is produced outside of the U. S. and appears to be a close analog of the C12 branched Na salt. However, no test data are provided for this substance either in the test plan or IUCLID Data Set, nor is an explanation provided for its inclusion. Otherwise, the category definition is adequate.

Category Justification

The submitter supports the ADPODS category on the basis of structural similarity; similar or incremental changes in the physicochemical, environmental fate, ecological and mammalian toxicological properties of these substances; and common precursors and/or degradation products. In general, the values provided by the submitter for the environmentally important physicochemical properties are either similar or show a regular trend with increasing alkyl side-chain carbon number. Since these compounds are chemically stable in water and water-soluble, and will not volatilize significantly (aromatic sulfonic acids are typically ionized at environmental pH), the predominant mode of degradation will be biodegradation. Data from ecotoxicity studies generally show an inverse correlation of the LC_{50} values with increasing carbon number of the alkyl side chains. Finally, mammalian toxicity data also support the ADPODS category based on similar acute, subchronic/chronic, and genetic toxicities.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility).

The data provided in the test plan for melting point, boiling point, vapor pressure and octanol/water partition coefficient are adequate for the purposes of the HPV Challenge Program.

Water solubility. The submitter stated in the test plan that sufficient data are available and no further testing for physicochemical properties is proposed. In Appendix A of the test plan, the submitter stated that the C6 linear sodium salt was miscible with water in a 1:1 (w/v) ratio. For the remaining six chemicals, the submitter provided >100,000 mg/L as the water solubility. For the C10 linear acid, the submitter noted that this water solubility is based on formulation. For the other five substances, the submitter noted that water solubility was determined using ACD/LogD estimation. Furthermore, in Appendix B, the submitter indicates that the water solubility data were calculated for 6 of the 7 chemicals. This appears to be an error. According to the robust summaries, the water solubilities were not estimated using the ACD/LogD program, but were estimates based on product formulation. The submitter needs to address the inconsistencies.

Estimated (WSKOW v1.40) water solubilities determined by EPA based on estimated log K_{ow} values range from 0.027 mg/L (for C16 linear sodium salt) to 3330 mg/L (for C6 linear sodium salt), which are significantly lower than the values provided by the submitter. The submitter's estimates based on product formulation information might not be appropriate, since product formulation could contain chemicals intended to solubilize the substance. In addition, since the chemicals in this category are used as surfactants and contain one or two long alkyl chain (>= C6) groups on either aromatic ring, they are expected to have low water solubilities. Therefore, the submitter needs to provide measured water solubility data for representative chemicals in this category following OECD guidelines. If the nature of

these chemicals makes experimental determination impractical, then the submitter needs to provide

estimated data using EPIWIN or other estimation programs.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

Photodegradation. EPA agrees with the submitter that since the category members have very low vapor pressures, they will not likely be found in air and testing is not needed for this endpoint. However, the submitter needs to incorporate this information in each robust summary.

Stability in water. EPA agrees with the submitter that these chemicals are not expected to undergo hydrolysis. However, the submitter needs to incorporate this information into the robust summary for each chemical.

Biodegradation. For the C10 linear sodium salt, the ready biodegradation data following OECD Guideline 301 E are adequate, but the data submitted for the C12 linear sodium salt and for the C12 branched sodium salt are not adequate for the purposes of the HPV Challenge Program. The inherent and semi-continuous activated sludge (SCAS) tests for these two chemicals highly favor biodegradation. For these two chemicals, the submitter needs to provide ready biodegradation data following OECD Guideline 301. The use of data for the C10 linear sodium salt and C12 branched sodium salt for the corresponding acids is acceptable.

In Appendix A of the test plan, the submitter indicates that all these chemicals are biodegradable. The way the information is presented may be misleading. For example, in the robust summary, the submitter indicates that the C10 linear sodium salt is not readily biodegradable. However, in Appendix A of the test plan, the submitter indicates that this chemical and its corresponding acid are biodegradable under SDA criteria, which is a SCAS test. This type of test is not adequate for the purposes of the HPV Challenge Program because it provides an optimal environment for biodegradation to occur. The submitter makes this same conclusion for the C12 linear sodium salt, when in fact, the only study provided is also for a SCAS test. In Appendix A, the submitter should not make any qualitative conclusions on the biodegradation of these chemicals.

Transport and distribution. The submitter proposes to conduct Level I fugacity modeling on the compounds at the boundaries of the category, the C6 linear sodium salt and the C16 linear sodium salt. EPA believes that providing data on only these two linear chemicals would not provide a complete picture on the fugacity of all the chemicals in the category. The submitter also needs to provide fugacity data on the C12 branched sodium salt. Although EPA had previously recommended the use of EQC Level I, this model is somewhat limited. EPA now recommends the use of EQC level III. EPA believes that values based on a level III fugacity model are more realistic and useful for estimating a chemical's fate in the environment on a regional basis. When developing the fugacity estimations, the submitter needs to use as much measured data as possible. The use of estimated values introduces uncertainties that then become magnified in modeling applications.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Adequate data are available for the category for acute, repeated-dose and genetic toxicities for the purposes of the HPV Challenge Program. EPA agrees with the submitter's plan to test C6 linear sodium salt and C16 linear sodium salt to represent the category for the reproduction/developmental endpoints and recommends a combined reproduction/developmental toxicity screening test (OECD TG 421), instead of the proposed combined repeated-dose/reproduction/developmental toxicity screening test (OECD TG 422). The submitter needs to address deficiencies in the robust summaries.

Reproduction toxicity. No reproductive toxicity studies are available. In Appendix B, the submitter has documented evaluations of the reproductive organs from the repeated-dose toxicity studies.

The submitter incorrectly reported the developmental toxicity (Chernoff Test) data on C6 linear sodium salt

under this endpoint. This summary needs to be placed in the developmental toxicity section of the robust summaries.

Developmental toxicity. The test plan does not specifically address the developmental toxicity endpoint. This omission needs to be corrected. The Chernoff Test data on C6 linear sodium salt are too limited to adequately address the endpoint.

Ecological Effects (fish, invertebrates, and algae).

The submitter proposed acute daphnia tests on C10 linear acid and on C12 branched acid because of "some inconsistency in daphnia data". EPA believes this testing is unnecessary because adequate invertebrate data are available. Any inconsistencies may be explained by providing the missing elements such as chemical composition and percent active ingredient. It should also be noted that water hardness strongly influences the aquatic toxicity endpoints for all surfactants and therefore is critical in interpreting the data and trend in toxicity across category members.

Fish. Overall the aquatic acute toxicity to fish is well supported in the test plan (data are available for C6, C10, and C12 linear sodium salts and C12 branched sodium salt); however, the submitter needs to provide a few missing data elements in the robust summaries. In addition, the submitter is encouraged to review the guidance on developing robust summaries (available at: http://www.epa.gov/chemrtk/robsumgd.htm) and consider revising the robust summary for the 96-hour study of C16 linear sodium salt in *Salmo gairdneri*.

Invertebrates. Adequate data were presented for acute studies for C6 and C12 linear sodium salts. The submitter is encouraged to review the guidance on developing robust summaries (available at: http://www.epa.gov/chemrtk/robsumgd.htm) and consider revising the robust summary for C16 linear sodium salt.

Chronic invertebrate. The submitter did not provide any chronic invertebrate data for the longer alkyl chain category members where EPA considers chronic toxicity to aquatic organisms may occur. The submitted 21-day chronic study on C16 linear sodium salt was considered inadequate because the reported LOEC was higher than the EC50 value and a measured concentration was provided only for the NOEC (the measured concentration was 30% less than nominal). In addition, the number of offspring, number of young per controls, and percent deaths for all concentrations of the 21-day chronic study were not reported. EPA requests a full robust summary containing all test information be submitted; otherwise, a daphnia chronic study on the C12 branched sodium salt will be needed to satisfy this endpoint.

Algae. While adequate algal toxicity data were provided for C6 and C16 linear sodium salts, there were no adequate data available on the critical mid-range C10 and C12 category members due to unreported algal EC50 values and longer than required test durations without interim analytical monitoring. This endpoint should be addressed by testing the C12 sodium salt.

Specific Comments on the Robust Summaries

Physicochemical Properties.

Vapor pressure. In all the robust summaries except that for C6 linear sodium salt, the submitter presents vapor pressure values less than zero (< 0). As negative values for vapor pressure do not exist, the submitter needs to incorporate in its robust summaries the vapor pressure values presented in Appendix A of the test plan.

Environmental Fate.

Biodegradation. In the robust summary for C10 linear sodium salt, in the first biodegradation study, the submitter indicates that this chemical has a degradation of < 100 % after 28 days. Such an imprecise value is not acceptable for this endpoint. The submitter needs to provide a specific value.

Health Effects.

Acute toxicity. C12 linear sodium salt and C12 branched acid. Robust summaries of the critical study did not report gross pathologic examination results.

Repeated-dose toxicity. C12 branched sodium salt. A robust summary for a 90-day feeding bioassay in rats lacks of information on ophthalmoscopic, neurobehavioral, hematology, clinical chemistry and urinalysis examination.

C16 linear sodium salt. A broader list of the organs/tissues examined histopathologically for a 90-day feeding bioassay in rats is provided in Appendix A of the test plan. The submitter needs to include this information in the robust summary.

Ecological Effects.

The submitter needs to provide percentages of the dialkyl components of the test substance where applicable or state clearly that test material has no dialkyl component. In addition, the submitter needs to provide the percentage of active ingredient where applicable in all key studies.

Fish. Commonly missing study details included test substance purity, water hardness, the number of concentrations tested, control use and response data, and the statistical methods used.

Invertebrates. Commonly missing study details included test substance purity, number of organisms per concentration tested, water hardness, water temperature, dissolved oxygen, number of concentrations tested, control use and response data, and statistical methods used.

Algae. Commonly missing study details included the test substance purity and control response data.

Followup Activity

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.